II. REMARKS

Claims 1 to 22 are pending in the subject application. Claims 2, 3, 5-9, 12 and 14 to 22, have been withdrawn from consideration as a result of a requirement for restriction. Claims 1, 4 and 10 to 13 are pending and were examined in the November 19, 2003 Office Action.

In view of the preceding amendments and reply, reconsideration and withdrawal of the objections rejections set forth in the November 19, 2003 Office Action is respectfully requested.

Objection To The Specification

The Office objected to disclosure because of the following informality: The definition of R^4 at page 14, paragraph 0058 appears to be misplaced since there is no previous reference to this radical. Correction or a clearer description is required.

In response to the Office's request, the paragraph has been moved to more clearly point out that R^4 is intended to define the structure present in paragraph [0061]. In view of this amendment, reconsideration and withdrawal of the objection is respectfully requested.

35 USC § 112

Claims 1, 4, 10, 11 and 13 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for phosphoramidatyl deoxyuridine compounds which fall within the scope of NB 1011, allegedly does not reasonably provide enablement for all phosphoramidatyl deoxyuridine compounds. The specification also was alleged to fail to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Office argued that Applicant admits at page 1, paragraph 0004 to page 2, paragraph 0005 that various biological pathways **may** be inactivated by tumor suppressing drugs. The Office noted that Applicants "have provided exemplary evidence that compounds within the scope of NB 1011 provide such an effect when treating rheumatoid arthritis."

The Office concluded that therefore, Applicant's generic claim to all phosphoramidatyl deoxyuridine compounds is deemed to be beyond the scope of the enabled disclosure of the specification.

Applicant respectfully traverses. Applicant's undersigned attorney respectfully requests clarification of the grounds of rejection. The cited paragraphs of Applicant's disclosure notes that "[f]unctional loss of tumor suppressor genes also has been linked to hyperproliferative inflammatory or autoimmune diseases that have cellular hyperproliferation as one of their characteristics.... These include rheumatoid arthritis, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma."

Thus, Applicant notes in the background that loss of p53 tumor suppressor function has been reported to contribute to the pathogenesis of rheumatoid arthritis (RA) and other autoimmune disorders. For example, Han et al. (1999)[1] (copy enclosed) noted that specific mutations of the p53 gene were reported to occur in erosive rheumatoid synovium and in culture fibroblast-like synoviocytes and that these specific mutations were previously found in neoplastic tissue. However, until the time of Applicant's invention, it was unknown nor predictive whether NB 1011 would suppress RA and other autoimmune disease. Applicant exemplifies in the subject specification that NB 1011 suppresses RA in an animal model shown to be predictive of clinical success. Previously, Applicant's NB 1011 compound, derivatives and analogs thereof, were shown to inhibit growth of neoplastic cells and tumors that also lack p53 gene tumor suppressor function (like RA). *See* PCT/US00/20008. In view of this information, the showing of the activity of NB 1011 as a therapy for RA (in the subject specification) enables the use of analogs and derivatives of NB 1011 to treat or suppress autoimmune disorders like RA since each disorder is linked to the loss of p53 tumor suppressor gene function.

In view of these remarks, reconsideration and removal of the rejection of the claims under 35 U.S.C. § 112, first paragraph is respectfully requested.

---

[1] Han et al. (1999) "Dominant-Negative p53 Mutations in Rheumatoid Arthritis" Arthritis & Rheumatism Vol.**42(6)**:1088-1092.

III. CONCLUSION

If a telephone interview would advance prosecution of the above-identified application, the Examiner is invited to telephone the undersigned attorney at the number provided below. Additionally, if the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 2518**, referencing No. 7008412001. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: May 19, 2004

By: _____
Antoinette F. Konski
Reg. No. 34,202

Bingham McCutchen LLP
Three Embarcadero Center, Suite 1800
San Francisco, California 94111
Telephone: (650) 849-4950
Telefax: (650) 849-4800